## AMENDMENTS TO THE DRAWINGS

Please replace Figs. 3A-3B, 4A-4C, 5, 6A-6C, 7A-7B, 8A-8D, and 12A-12B filed on November 15, 2004 with Figs. 3A-3B, 4A-4C, 5, 6A-6C, 7A-7B, 8A-8D, and 12A-12B submitted herewith.

**REMARKS**

This submission is in response to the Official Action dated February 23, 2005. Reconsideration of the above identified application, in view of the above amendments and the following remarks, is respectfully requested.

## I. Status of the Claims

Claims 1-3 have been amended. Claims 4-9 have been canceled without prejudice or disclaimer of the subject matter therein. Applicant requests the addition of new claims 10-56. No new matter is added. Claims 1-3 and 10-56 (50 claims) are pending. Claims 1-9 stand rejected.

Claims 1-3 have been amended to recite a system for modeling macroscopic characteristics of bone in which components that make up a first order macroscopic region of bone are nonhomogeneous. Support for this amendment is found in the Specification, e.g., paragraphs [0036]-[0037].

New claims 10, 11, 19-22, 29, 30, 41-45, and 48 are directed to models that include a third hierarchical order including one or more collagen bundles, hydroxyapatite crystallites, mucopolysaccharides, or combinations thereof. Support for these claims is found in the Specification, e.g., paragraphs [0105]-[0106].

New claims 12 and 31 are directed to models in which the third order components are anisotropic. Support for these claims is found in the Specification, e.g., paragraphs [0036]-[0037] and [0099].

New claims 13, 32, and 46 recite an external force that is applied to a macroscopic region of the bone and the model is used to determine a response to the external force. Support for these claims is found in the Specification, e.g., paragraphs [0036]-[0037].

New claims 14-18, 25, 26, 33-40, 48, 51, 53, and 54 are directed to models in which mechanical properties of components of the bone are assigned based on experimental determinations. Support for these claims is found in the Specification, e.g., paragraphs [0079], [0103], [0107], [0119]-[0124], and [0138]-[0151].

New claims 19-22, 26, 41-44, and 54 are directed to models in which mechanical properties of the second order components are based on the orientation directions of the third order components. Support for these claims is found in the Specification, e.g., paragraphs [0074], [0100] and [0113]-[0114].

New claims 23 and 46-50 are directed to models in which boundary conditions are assigned to the third order components to characterize relative ability to move under loading. Support for these claims is found in the Specification, e.g., paragraphs [0060] and [0106].

New claims 24, 25, 52, and 53 are directed to models in which a relative amount of the third order components depends on degree of calcification of the second order components. Support for these claims is found in the Specification, e.g., paragraphs [0004], [0094], and [0098].

New claims 27 and 55 are directed to models in which second order components include voids representing canaliculae, lacunae, or combinations thereof. Support for these claims is found in the Specification, e.g., paragraph [0166].

New claim 28 is directed to a method of producing a hierarchical model of bone in which the mechanical properties of second order components are used to determine a mechanical property of a first order macroscopic region of bone. Support is found in the Specification, e.g., paragraphs [0050]-[0051] and [0105]-[0106].

## II. Supplemental Information Disclosure Statement

Applicant submits, concurrently with this Amendment, a Supplemental Information Disclosure Statement that complies with 37 C.F.R. § 1.98(a)(2) and copies of the cited references

as attachments thereto. Consideration of these references and acknowledgment by initialing the Form SB/08 is respectfully requested.

## III. Status of the Drawings

The Drawings have been objected to for having inadequate margins. Applicant submits herewith replacement sheets with Figs. 3B, 4C, 6B, 6C, 7B, 8D, and 12B in order to correct the size of the margins, as requested by the Examiner. Based on the foregoing, Applicant respectfully requests the above objection be withdrawn.

## IV. 35 U.S.C. § 112 Rejection (Written Description and Enablement)

Claims 1-9 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner states that the Specification does not convey that the inventor had possession of the invention as claimed and does not enable one skilled in the art to make and/or use the invention (Office Action dated February 23, 2005, pages 2-9). Applicant respectfully traverses this rejection, and reconsideration is respectfully requested.

Regarding points 4.1 and 5.1 of the Office Action, the Examiner rejected claim 5 for reciting three orders of hierarchical properties of the microstructure of the bone, wherein one of the orders comprises a macroscopic region of the bone. The Examiner states that it does not make sense that the microstructure of bone would include the macrostructure of bone.

Claim 5 has been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claim 5 has been rendered moot. Claim 1, on which claims 2 and 3 depend, has been amended to recite two orders of hierarchical properties "of the bone," and not specifically, "of the microstructure of the bone." In other words, the microstructure contributes to the macrostructure. As amended, the claims clarify the relationship between the three orders of hierarchy. New claims 10-55 do not state that the microstructure of bone includes the macrostructure of bone.

Regarding points 4.2-4.5 and 5.2-5.5 of the Office Action, the Examiner rejected claims 6-9 for not explaining how one can compare a mathematical model with a subject bone. Thus, it is not possible to "compare the mathematical equations [written on a paper or incorporated into software] to the subject bone or an actual or real or human bone." Furthermore, regarding claim 6, the Examiner states that it is not clear how deformation or fractures are predicted based on differences in the model and the subject bone.

Claims 6-9 have been canceled without prejudice or disclaimer of the subject matter therein. Hence, the rejection of claims 6-9 has been rendered moot. Without conceding to the Examiner's arguments, the new and amended claims do not state that a mathematical equation is "compared" to a subject bone in the direct or invasive sense apparently implied by the Examiner. The claims set forth a system and method of producing a model of bone by which the mechanical behavior of a real bone can be predicted, based on data and calculations from experiments on representative subject bones of the same type and pathology. This is an empirically based model. The real bone can be compared with the model to estimate real world behavior. A "virtual" bone can be constructed based on data from a population of like bones, which in turn can be compared to patient-specific data, for example to evaluate patient-specific interventions. Further, the language questioned by the Examiner does not appear in the pending claims.

Based on the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

## V. 35 U.S.C. § 101 Rejection

Claims 1-9 have been rejected under 35 U.S.C. § 101 for being directed to nonstatutory subject matter. Applicant respectfully traverses this rejection, and reconsideration is respectfully requested.

The Examiner rejected claims 1-9 for being directed to a set of mathematical equations or a software tool and contends that such subject matter is nonstatutory. The Examiner also rejected claims 4-9 for reciting a method that is not directed to the technological arts. The

Examiner stated that claims 4-9 do not describe any type of computer-implemented steps (Office Action dated February 23, 2005, page 10). Claims 4-9 have been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claims 4-9 has been rendered moot.

Claims 1-3 have been amended and claims 10-27 have been added. These new and amended claims set forth a system for modeling macrostructural characteristics of a bone. New claims 28-55 recite a method of producing a model of a bone. The Examiner apparently argues that, to be statutory, the claims must recite a system or apparatus with expressly recites hardware and software components, and that method claims must recite computer-implemented steps. Applicant respectfully disagrees.

The claims include, but do not require, computer implementation. The model is not necessarily computerized in all embodiments of the invention, nor is every step a computer function. A person of ordinary skill in the art will appreciate that a computer implementation is preferred, and the use of a super-computer may be particularly preferred in those embodiments which employ finite element analysis. These techniques are known. In any case, the claimed system and method applies a step-by-step procedure that can, but need not be, performed by a machine such as a computer. Though laborious, a model can be created "by hand," i.e., without using computer hardware or software. As set forth in independent claims 1 and 28, the system and method includes two hierarchical orders of bone with components of the second order being used to construct a first order macroscopic region of the bone. A property of the first order region can be determined from these mechanical properties. Calculations can be done by hand if desired, and without computer hardware or software. It is not necessary to recite any hardware or software components in the claims. It is sufficient that the claimed steps are performed, or that the elements of the claimed system are present in relation to each other, as claimed.

A system or method implemented "by hand" is patentable. That some steps encompass calculations or comparisons does not mandate the use of a computer or implementation by hardware and software.

In *Alco Standard Corp. v. TVA*, 808 F.2d 1490, 1496 (Fed. Cir. 1986), the court held that a process that is capable of being performed by a person or by a machine is patentable. Appellants contended that steps of "correlating and combining" data were "merely mental processes, and therefore, unpatentable." *Id.* at 1496. However, the court stated that "[u]nder the meaning of correlating used in the patent, these steps may be performed either by a person or by a machine... The inclusion in a patent of a process that may be performed by a person, but that also is capable of being performed by a machine is not fatal to patentability" *Id.*, citing *Diamond v. Diehr*, 450 U.S. 175 (1981).

Furthermore, a claim that has a practical application in the technological arts is statutory (MPEP § 2106, paragraph IV.B.2(a), page 2100-15). The Examiner states that (emphasis added):

> To be statutory, the utility of an invention must be within the technological arts. *In re Musgrave*, 167 USPQ 280, 289-90 (CCPA, 1970). The definition of "technology" is the "application of science and engineering to the development of machines and procedures in order to enhance or improve human conditions, or at least to improve human efficiency in some respect." (Computer Dictionary 384 (Microsoft Press, 2d ed. 1994)). (Office Action dated February 23, 2005, page 10.)

Clearly the invention provides procedures to enhance and improve human conditions, i.e., modeling bone to assess bone deformations, to compute stresses and strains due to specific forces acting on bone and to predict forces that do or do not cause viscous effects or elastic or plastic bone deformations.

The MPEP also states that an example of a type of claimed statutory process is "[a] digital filtering process for removing noise from a digital signal comprising the steps of calculating a mathematical algorithm to produce a correction signal and subtracting the correction signal from the digital signal to remove the noise" (MPEP § 2106, paragraph IV.B.2(b)(ii), page 2100-18). Clearly, this exemplary statutory process sets forth a mathematical algorithm including calculations, but does not set forth any machine, e.g., computer hardware or software components.

A machine or method claim is statutory when the machine or method, as claimed, "produces a concrete, tangible and useful result" (MPEP § 2106, paragraph IV.B.2(b)(ii), page 2100-18, citing *AT&T Corp. v. Excel Communications, Inc.*, 172 F.3d 1352, 1358 (Fed. Cir. 1999) and *State Street Bank & Trust Co. v. Signature Financial*, 149 F.3d 1368, 1373 (Fed. Cir. 1998)). The invention set forth in the pending claims includes a transformation of data to produce a useful, concrete, and tangible result. For example, a transformation of data occurs when the mechanical properties of the second order components are used to determine a mechanical property of the first order region of macroscopic bone. This transformation of data produces a useful, concrete, and tangible result which is the mechanical properties of the first and second order components. These mechanical properties are used to study or predict the behavior of the bone, e.g., when it is subject to an external force. The predictions of the behavior of bone can be used, for example, to improve the fitting of implants. The behavior of the bone subject to the external force can also be used to study deformation and fracture in the bone.

For the aforementioned reasons, the subject matter of the claims is statutory with or without the recitation of computer hardware or software components.

Based on the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn, and reconsideration is respectfully requested.

## VI. 35 U.S.C. § 103(a) Rejections

### *A. Crolet, Lakes, and Manolagas (Claim 1)*

Claim 1 has been rejected as being obvious and unpatentable over Crolet, "Compact Bone: Numerical simulation of mechanical characteristics," 26 J. Biomechanics 677-687 (1993) ("Crolet"), in view of Lakes, "Materials with structural hierarchy," Nature, 361 (1993) ("Lakes"), and further in view of U.S. Patent No. 6,416,737 to Manolagas et al. ("Manolagas"). Applicant traverses this rejection, and reconsideration is respectfully requested.

Claim 1 has been amended and is directed to a system for modeling macrostructural characteristics of a bone. The system includes at least two inter-related orders of hierarchical structural and hierarchical mechanical properties. The first order comprises at least one macroscopic region of the bone. The second order is non-homogeneous and, in preferred embodiments, comprises at least one or more osteons, trabeculae, or lamellae all of which vary in degree of calcification and collagen fibril orientation. The second order components are used to construct the first order macroscopic region, i.e., to estimate its mechanical behavior. Mechanical properties can be determined experimentally. Thus, data from a set of samples can be used to represent a subject bone of a selected type, according to the steps of the claims.

Claims 1-3 have been amended in particular to clarify that second order components (e.g., osteons, trabeculae, or lamellae) are non-homogeneous. The second order components are non-homogeneous with respect to degree of calcification and anisotropic with respect to collagen orientation. This is not found in the cited references. New claims 10-27 depend from claim 1 and also include this feature. New claims 28-55 also recite that the second order components comprising the osteons, trabeculae, or lamellae are non-homogeneous. The advantages of incorporating non-homogeneity in the second order components of the bone model are described in paragraph [0037] of the Specification:

> Morphological and mechanical studies of bone show that at all hierarchical levels bone is anisotropic (the local mechanical properties are direction dependent), and non-homogeneous (the structure is not the same at different points). Nevertheless to simplify bone modeling, bone structure often is assumed to be homogeneous, isotropic (not direction dependent), transversely isotropic (one plane of symmetry), or orthotropic (three planes of symmetry). The simplifications of isotropy, orthotropy, and transverse isotropy give rise to unrealistic models because these simplifications that symmetries that do not exist. For instance, in such models stresses may be over- or under-estimated. When such models are applied to practical applications, for example bone implants, poor estimates of stress may give rise to screw loosening in implants.

Modeling at least the second order components of the bone structure as non-homogeneous, and doing so as described and claimed herein, e.g., using representative empirical data, provides an improved bone model, unlike the simplified models provided in the prior art.

New claims 10, 11, 19-22, 29, 30, 41-45, and 48 state that the third order comprises at least one component representing one or more collagen bundles, hydroxyapatite crystallites, mucopolysaccharides, or combinations thereof. A mechanical property is correlated to each of the third order components. The third order components are used to construct the second order components including an estimation of their contribution to second order mechanical properties.

Before this amendment, claim 1 stated that the model had a three-order hierarchical structure and that the model comprised interactions with an external force. The Examiner contends that Crolet and Lakes disclose models of bone with a three-order hierarchical structure. The Examiner also states that Crolet does not disclose a model comprising interactions of the bone with external force, but that Manolagas teaches that bone can be distorted permanently by application of an external force. The Examiner states that the Manolagas reference suggests that it would be desirable to modify Crolet's model to assess how the bone would respond to an external force (Office Action mailed February 23, 2005, page 28).

In response to the previous Office Action mailed July 16, 2004, Applicant stated that Crolet presumes that the entire osteon is homogeneous. Crolet teaches a simplified model of bone because it disregards the non-homogeneity of the structure (Crolet, p. 679). Specifically, Crolet teaches a theory of bone macrostructure which presumes there are uniform collagen fibrils in the osteons, thereby resulting in osteons that are homogenous, i.e., a simple average. Crolet models a lamella by dividing it into identical cylindrical sectors. The mechanical properties of other sectors may be computed from knowing the mechanical properties of one sector and rotating it (Crolet, p. 679). The characteristics of one sector are "sufficient to determine the mechanical homogenized behavior of all the lamellar sectors" (Crolet, p. 680). This is different from the claimed invention, which does not presume this simplified behavior and instead empirically maps mechanical properties into each hierarchical order of bone in a non-homogeneous manner, as claimed. As set forth in claims 14-18, 25, 26, 33-40, 48, 51, 53, and 54, these mechanical properties can be determined experimentally based on measurements from mechanical testing of subject bones and incorporated into the bone model.

Crolet also does not incorporate variations in the third order of bone hierarchy into its model, as claimed here, to form non-homogeneous second order components. Claims 10, 11, 19-22, 29, 30, 41-44, and 48 expressly state that the second order components are comprised of third order components. Crolet acknowledges that real bone has three orders of hierarchical structure, but Crolet does not examine the third order microstructure to form a model. Since Crolet's lamellae, i.e., second order components, are constructed by repeating identical lamellar sectors, Crolet's second order structures are homogeneous and uniform. Therefore, unlike the claimed invention, mechanical properties are not assigned to the third order components (e.g., collagen bundles or orientation, hydroxyapatite crystallites, mucopolysaccharides, calcificatoin, or combinations thereof). Crolet does not construct a more detailed model using non-homogeneous and anisotropic second order structures (e.g., osteons, trabeculae, or lamellae), from which first order predictions of bone behavior are made.

New claims 12 and 31 state that the second order components are anisotropic. In the Office Action mailed February 23, 2005, the Examiner stated that Lakes discloses a model of bone that incorporates the anisotropy of lamina. Thus, as understood, the Examiner responded to Applicant's argument regarding Crolet's oversimplification by arguing that it would be obvious to modify Crolet's model to incorporate the anisotropy of Lakes and then further borrow from Manolagas to evaluate responses to applied force. Respectfully, this appears to be hindsight, based on the invention and Applicant's arguments. Lakes does not provide what is missing from Crolet. Lakes acknowledges that in nature osteons and lamellae are anisotropic and that collagen orientation is one reason for this. However, Lakes does not use this observation to study or predict the macroscopic behavior of a subject bone, and does not suggest to do so, nor say how to do so - all in contrast to the present disclosure and particularly the new and amended claims.

Lakes discloses a hierarchical structure in which fibers are embedded in a matrix to form anisotropic sheets or laminae, which are bonded together to form a laminate (Lakes, p. 2, lines 13-15). However, Lakes does not disclose that the osteons are nonhomogeneous, nor how to account for this in a bone model. Lakes merely teaches that bone has a hierarchical structure as shown in Figs. 2 and 4, but does not teach or suggest how to incorporate the hierarchical

structure into a model of bone that includes nonhomogeneous and/or anisotropic second order components. Lakes also does not disclose how to use the mechanical properties of the second order components to determine a mechanical property of a macroscopic region of bone, as set forth in the new and amended claims. Lakes does not use the anisotropy of third order components to determine the mechanical properties of second order components, as set forth in claims 12 and 31. Unlike the claimed invention, Lakes does not disclose that mechanical properties are assigned to third order components in order to construct a model using non-homogeneous and/or anisotropic second order structures (e.g., osteons, trabeculae, or lamellae), from which first order predictions of bone behavior are made. See claims 10, 11, 19-22, 29, 30, 41-45, and 48. Lakes also does not disclose that the mechanical properties of second or third order components are determined experimentally based on measurements from mechanical testing of subject bones and incorporated into the bone model. See claims 14-18, 25, 26, 33-40, 48, 51, 53, and 54.

Moreover, as set forth in claims 19-22, 26, 41-44, and 54, the orientation directions of the third order components, e.g., collagen bundles, are used to determine the mechanical properties of the third order components. The model of the invention incorporates information regarding the distribution of dominant collagen bundle directions (paragraphs [0043], [0048], [0094] of the Specification). As recited in claims 22 and 44, the osteons included in the model are alternate, extinct, and bright osteons. These osteon types correspond to different collagen bundle patterns in fiber orientation in successive lamellae (paragraph [0113] of the Specification). Extinct osteons include extinct lamellae formed by alternating layers of collagen bundles with orientation directions of about 82° and -82°. Alternate osteons include lamellae in successive layers with orientation directions in sequence of about -61.5°, -41°, -20.5°, 0°, 20.5°, 41°, and 61.5° (paragraph [0168] of the Specification). Crolet does not disclose or suggest that collagen orientation varies with each lamella.

New claims 24, 25, 52, and 53 are directed to models in which a relative amount of the third order components depends on degree of calcification of the second order components (paragraphs [0004], [0094], and [0098] of the Specification). Crolet and Lakes do not disclose or

suggest that the degree of calcification of the second order components varies or that the degree of calcification can be measured experimentally.

As set forth in claims 14-18, 25, 26, 33-40, 48, 51, 53, and 54, mechanical properties are determined by experimentation (paragraphs [0100]-[0101] of the Specification) and are not a uniform mathematical simplification. The advantages of using experimental findings and incorporating them into the bone model are described in paragraph [0092] of the Specification:

> [T]his invention provides more realistic prediction than purely mathematical models, that is models based on hypotheses, which are not based on experimentation. The literature is full of research on bone microstructure, which employs purely mathematical models of osteon behavior (Pidaparti and Burr, 1992). Such approach is limited, often unrealistic and does not always predict biological phenomena. The invention is flexible so as to include new experimental findings of bone structural and mechanical properties. This ensures the invention's realistic characteristic insertion of prostheses, etc.

Thus, experimental findings using cadaveric bone can provide a model that is more detailed and will be an improved predictor of properties of a subject bone. The properties of cadaveric bone are determined by experimentation. As set forth in claims 15, 16, 21, 34, 35, and 43, the cadaveric bones can be chosen free of pathology or with a specific pathology, i.e., of a specific type, to apply the model to a specific condition or pathology (paragraphs [0012] and [0107] of the Specification).

In sum, the models provided by Crolet and Lakes do not disclose or suggest a bone structure model that incorporates non-homogeneous second order components to provide a more detailed model of macroscopic bone. The prior art models also do not disclose or suggest further incorporating third order properties, e.g., collagen orientation, into a bone structure model. Crolet and Lakes also do not disclose that representative properties are determined by experimentation or that the properties may be determined by experimentation for a specified type of bone, including bone pathology.

Manolagas discloses a method for increasing bone strength with selected bisphosphonates and therefore also does not disclose a method for modeling bone as set forth in the invention.

There is no motivation to use the Manolagas method for increasing bone strength to modify Crolet or Lakes. Testing whether a drug improves bone strength does not indicate a model based on applying force nor how to modify the simplified prior art models to study or predict bone behavior, nor how to incorporate non-homogeneity across two corresponding orders of bone hierarchy.

Hence, Crolet, Lakes, and Manolagas do not disclose or suggest all of the elements set forth in the claims, nor do their teachings make any of the claims obvious.

*B. Crolet, Lakes, Manolagas, and Jiang (Claims 2 and 4)*

Claims 2 and 4 have been rejected as being obvious and unpatentable over Crolet in view of Lakes and further in view of Manolagas and U.S. Patent No. 6,442,287 to Jiang ("Jiang"). Applicant traverses this rejection, and reconsideration is respectfully requested.

Claim 2 states that the bone is compact or cancellous bone. The Office Action contends that Crolet, Lakes, and Manolagas teach the bone model as recited in claim 1, and that Jiang teaches that the analysis of cancellous bone mass and structure enables the assessment of bone strength and allows the assessment of risk of fracture.

Jiang discloses a method and system for computerized analysis of bone mass and structure that can be used to analyze cancellous bone. Jiang uses images of a bone to estimate the strength of the bone. However, Jiang does not provide a model for predicting fracture or deformation. Furthermore, Jiang does not teach or suggest how to modify a model, such as the models provided by Crolet and Lakes, to compute fracture or deformation. Thus, like Crolet, Lakes, and Manolagas, Jiang does not disclose or suggest a model in which the components of the second order, e.g., the osteons, trabeculae, or lamellae, are non-homogeneous. Jiang also does not disclose a model that incorporates the hierarchical structure in which the mechanical properties of non-homogeneous second order components are used to predict the behavior of a first order macroscopic region of bone. There is no suggestion to use the methods of Crolet,

Lakes, or Manolagas to model cancellous bone per Jiang, nor would this provide the claimed invention.

As stated in paragraph [0007] of the Specification, cancellous bone consists of trabeculae, and "collagen fibrils run mostly parallel to the long axis of tubular trabeculae in the trabeculae outer portion and perpendicular in the inner portion." Thus, the model of the invention includes information regarding the collagen fibril orientation of cancellous bone as set forth in claims 19-22 and 41-44. Also, as stated in paragraph [0081] of the Specification, "cancellous bone has been described as continuous and isotropic, which does not reflect the high porosity and the changing details (such as collagen bundles direction and lamellar structure) at the microstructural level." The claimed model includes information such as the direction of collagen bundles and lamellar structure at the microstructural (third order) level to construct non-homogeneous and anisotropic second order components, which in turn are used to construct a first order macroscopic region of cancellous bone. Since Crolet's and Lakes' models do not incorporate third order information (e.g., regarding the distribution and orientation of collagen fiber bundles in bone) to construct non-homogeneous and anisotropic second order components, these references, with or without Jiang, do not provide the invention or make it obvious.

Furthermore, Applicant respectfully contends that the Examiner is improperly using hindsight to reconstruct the invention. There is no motivation to modify Crolet's or Lakes' bone models to model cancellous bone. Lakes actually teaches away from modeling cancellous bone using a fibrous laminate and instead teaches a model of cancellous bone comprised of cellular solids (Lakes, p. 6, "Cellular solids"). Thus, using Crolet and Lakes, one would be motivated to use cellular solids to model cancellous bone.

Claim 4 was directed to a method of predicting deformation and fractures of bone using the model of claim 1. The Examiner contends that Jiang discloses a method of predicting deformation and fractures. Claim 4 has been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claim 4 is moot.

New claims 46-50 set forth a method of producing a model of bone including the step of computing deformation and fractures of the bone. See also claim 23. The method comprises the steps of assigning a force acting on the selected bone and assigning boundary conditions of the third order components of the selected bone. The boundary conditions characterize movement of the boundaries of the third order components. The deformation or fractures are computed using the mechanical properties assigned to the third order components, the force acting on the selected bone, and the boundary conditions of the third order components of the selected bone. This combination of steps is not taught or obvious from the references.

The models of the prior art provide theoretical ways to model the bone, but do not disclose computing fractures or deformation using a model in which mechanical properties of third order components are used to contribute to and help predict the behavior of a first order macroscopic region of bone.

Claim 49 sets forth a method of producing a model of bone including the step of computing deformation and fracture based on the boundary conditions of the third order components, wherein the boundary conditions of the third order components located at an interface between the second order components are specified as having freedom of movement under loading. In claim 47, fracture lines are determined based on locations of cement lines formed between the second order components. Fracture lines follow the cement lines (paragraph [0054] of the Specification), and the fracture mechanism of bone also depends on bone structural and composition properties of the third order components such as collagen architecture and collagen content (paragraph [0077] of the Specification). See claims 46-50. As stated above, Crolet, Lakes, and Jiang do not account for such factors.

The references do not disclose or suggest all of the features of the invention, and respectfully, the obviousness rejection should be withdrawn, nor do the references apply to the new and amended claims.

*C. Crolet, Lakes, Manolagas, Winder, Ascenzi I to V (Claim 3)*

Claim 3 has been rejected as being obvious and unpatentable over a combination of eight references: Crolet in view of Lakes and further in view of Manolagas; U.S. Patent No. 6,213,958 to Winder ("Winder"); Ascenzi, "The tensile properties of single osteons," August 1965 ("Ascenzi I"); Ascenzi, "The shearing properties of single osteons," September 1971) ("Ascenzi II"); Ascenzi, "The torsional properties of single selected osteons," October 1993 ("Ascenzi III"); Ascenzi, "The first estimation of prestress in so-called circularly fibered osteonic lamellae," March 1999 ("Ascenzi V"); and Ascenzi, "Pinching in longitudinal and alternate osteons during cyclic loading," November 1996 ("Ascenzi IV"). Applicant traverses this rejection, and reconsideration is respectfully requested.

Claim 3 depends from claim 1 and states that the mechanical properties that correlate with each component are selected from the group consisting of tension, compression, shear, bending, torsion, prestress, pinching, and cement line slippage. The Office Action contends that Crolet, Lakes, and Manolagas teach the bone model described above, and that Winder and Ascenzi I to V teach all of the recited mechanical properties.

As noted above, Crolet, Lakes, and Manolagas do not disclose or suggest a model in which the components of the second order, e.g., the osteons, trabeculae, or lamellae, are non-homogeneous. Crolet, Lakes, and Manolagas also do not disclose a model that incorporates the hierarchical structure in which the mechanical properties of non-homogeneous second order components are used to help predict the behavior of a first order macroscopic region of bone.

Furthermore, Crolet and Lakes show only that mechanical properties of the bone can be measured; they do not teach or suggest incorporating mechanical properties into a model, nor measuring them for that purpose, as opposed to the simplified mathematical theories the references do apply.

As stated in response to the previous Office Action mailed July 16, 2004, it would not be obvious to modify Crolet using Winder and Ascenzi I to IV. The Examiner has not addressed

this argument. Specifically, Applicant stated that Crolet teaches simulation of mechanical behavior of all lamellae by "knowledge of the homogenized characteristics of only one [lamellae]" (Crolet, p. 680, col. 1, paragraph 4). Crolet further discloses simulation of osteon structure by using "only the mathematical theory of homogenization" (p. 680, col. 1, paragraph 5). This teaches away from the invention. Crolet makes no suggestion to modify its simplified mathematical model by using nonhomogeneous criteria or how to do so. Crolet also makes no suggestion to include mechanical properties, e.g., tension and prestress, shearing strength, torsional properties, and pinching. Crolet offers its uniform mathematical approach as sufficient to create a partial macrostructural model of bone, and thus would not teach one skilled in the art to incorporate practical measurements of experimental conditions, nor any properties disclosed in Ascenzi I to IV (e.g., calcium content and osteons having longitudinal arrangement versus osteons having alternate arrangement). Furthermore, the addition of Winder would not teach one skilled in the art to account for the hierarchical mechanical properties of bone, and correlate such mechanical properties with each component of the hierarchical structure of bone as claimed.

For the same reasons, it would not be obvious to modify Crolet using Ascenzi V (e.g., regarding prestress). Ascenzi V discloses a lamellar model for estimating prestress in osteonic lamellae, but the reference does not disclose or suggest incorporating the estimate of prestress in a bone model. The reference also does not disclose or suggest a bone model with a hierarchical structure and mechanical properties as in the claimed invention.

Neither Lakes nor Manolagas disclose that a model of bone can be modified to include mechanical properties, e.g., tension and prestress, shearing strength, torsional properties, and pinching. The references also do not provide motivation to modify a bone model to include these properties, nor say how to do so.

Thus, Crolet, Lakes, Manolagas, Winder, and Ascenzi I to V do not disclose or suggest all of the features of the invention.

*D. Crolet, Lakes, Manolagas, Copland, and Agrawal (Claim 5)*

Claim 5 has been rejected as being obvious and unpatentable over Crolet in view of Lakes and further in view of Manolagas, U.S. Patent No. 6,333,313 to Copland III et al. ("Copland"), and U.S. Patent No. 5,947,893 to Agrawal et al. ("Agrawal"). Claim 5 has been canceled without prejudice and the rejection is moot.

*E. Crolet, Lakes, Manolagas, Jiang, and Mazess (Claim 6)*

Claim 6 has been rejected as being obvious and unpatentable over Crolet in view of Lakes and further in view of Manolagas, Jiang, and U.S. Patent No. 6,517,487 to Mazess et al. ("Mazess"). Claim 6 has been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claim 6 has been rendered moot.

Note also that Mazess discloses a scanning device that uses ultrasonic acoustic signals to provide measurements of certain physical properties of bone. The Examiner contends that Mazess discloses comparing measurements from a subject bone with a model to predict possible fracture risk. Mazess does discloses a method for taking certain measurements of bone, but does not disclose providing a model of bone or incorporating the measurements or other experimental determinations into a model of bone. Mazess discloses comparing measurements taken from sending an ultrasonic pulse through a subject and comparing them to reference measurements taken from sending an ultrasonic pulse through a substance of known acoustic properties, such as water (Mazess, column 8, lines 55-59). Mazess then compares the transit time for the pulse and relates the time to physical properties and integrity of the bone (Mazess, column 9, lines 49-53).

Thus, Mazess merely takes measurements from a subject bone or from a substance of known acoustic properties, such as water. Mazess does not disclose a model of bone or predicting deformation or fractures of a bone based on a model of bone.

*F. Crolet, Lakes, Manolagas, Copland, Agrawal, Mazess, and Wood (Claim 7)*

Claim 7 has been rejected as being obvious and unpatentable over Crolet in view of Lakes and further in view of Manolagas, Copland, Agrawal, Mazess, and U.S. Patent No. 6,083,264 to Wood ("Wood"). Claim 7 has been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claim 7 has been rendered moot.

*G. Crolet, Lakes, Manolagas, Copland, Agrawal, Mazess, Healy, and Wood (Claim 8)*

Claim 8 has been rejected as being obvious and unpatentable over Crolet in view of Lakes and further in view of Manolagas, Copland, Agrawal, Mazess, U.S. Patent No. 6,692,532 to Healy ("Healy"), and Wood. Claim 8 has been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claim 8 has been rendered moot.

*H. Crolet, Lakes, Manolagas, Copland, Agrawal, Mazess, and Lee (Claim 9)*

Claim 9 has been rejected as being obvious and unpatentable over Crolet in view of Lakes and further in view of Manolagas, Copland, Agrawal, Mazess, and U.S. Patent Application Publication No. 2002/0136696 to Lee et al. ("Lee"). Claim 9 has been canceled without prejudice or disclaimer of the subject matter therein, and therefore, the rejection of claim 9 has been rendered moot.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: August 19, 2005

Respectfully submitted,

By Wh Poy

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